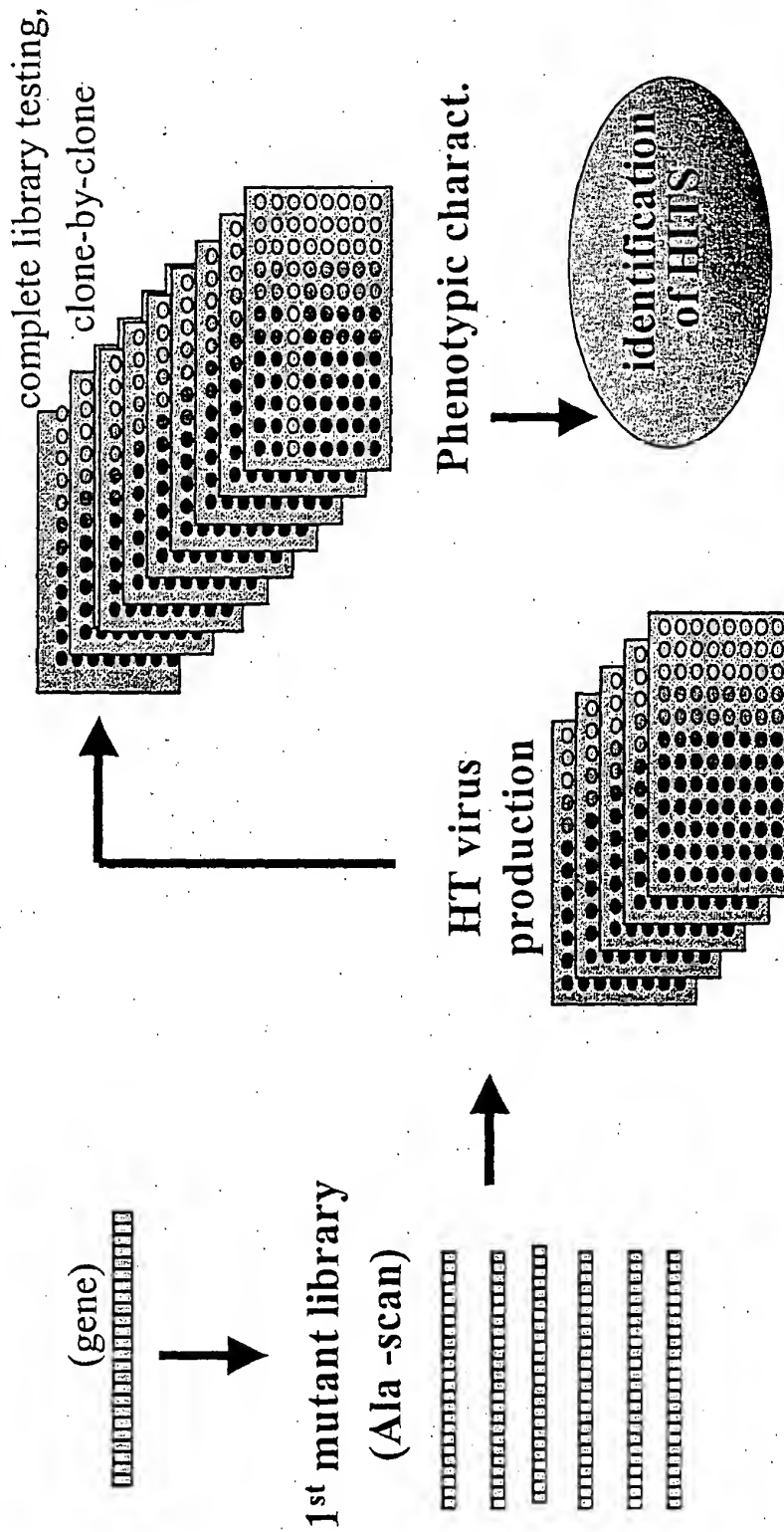


Fig. 1A

1st Round : screening of mutants (full length Ala-scan)



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FIG. 1B

2nd Round : screening of mutants at (surrounding) HIT positions

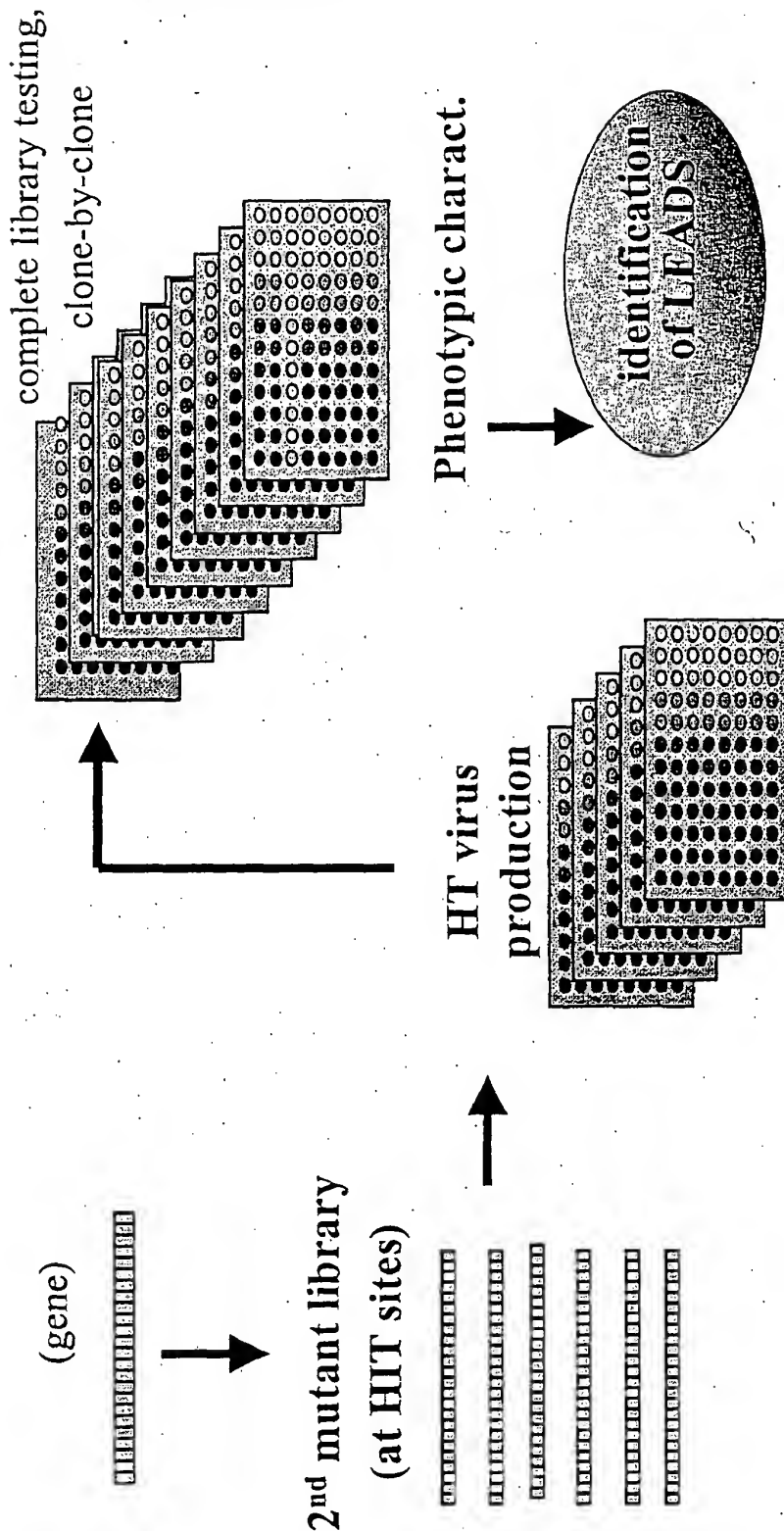


FIG. 1C

3rd Round : screening of recombinants between LEADS

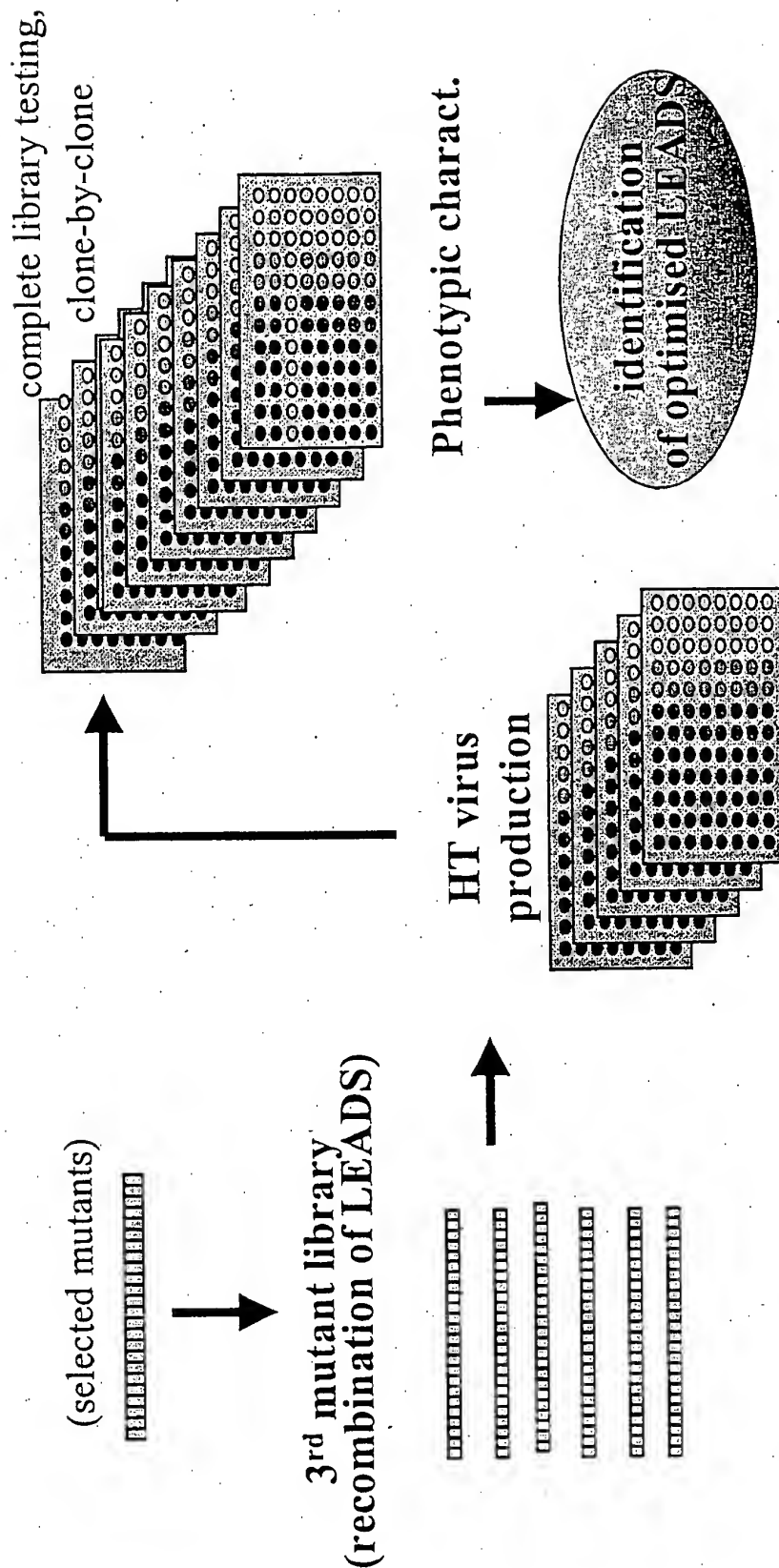
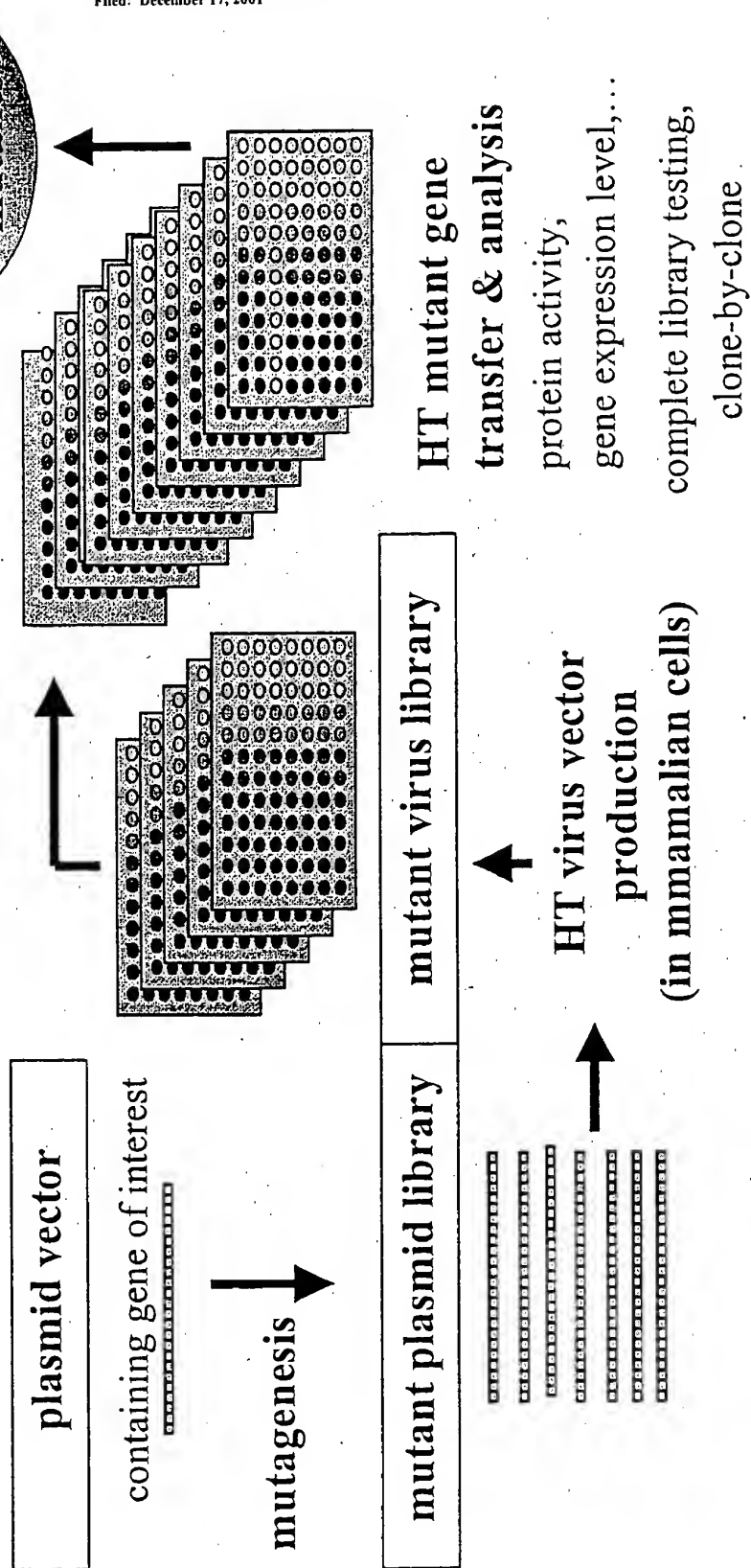


FIG. 1D

Gene optimisation (in mammalian cells)



F16. 1E

Gene optimisation (in bacteria)

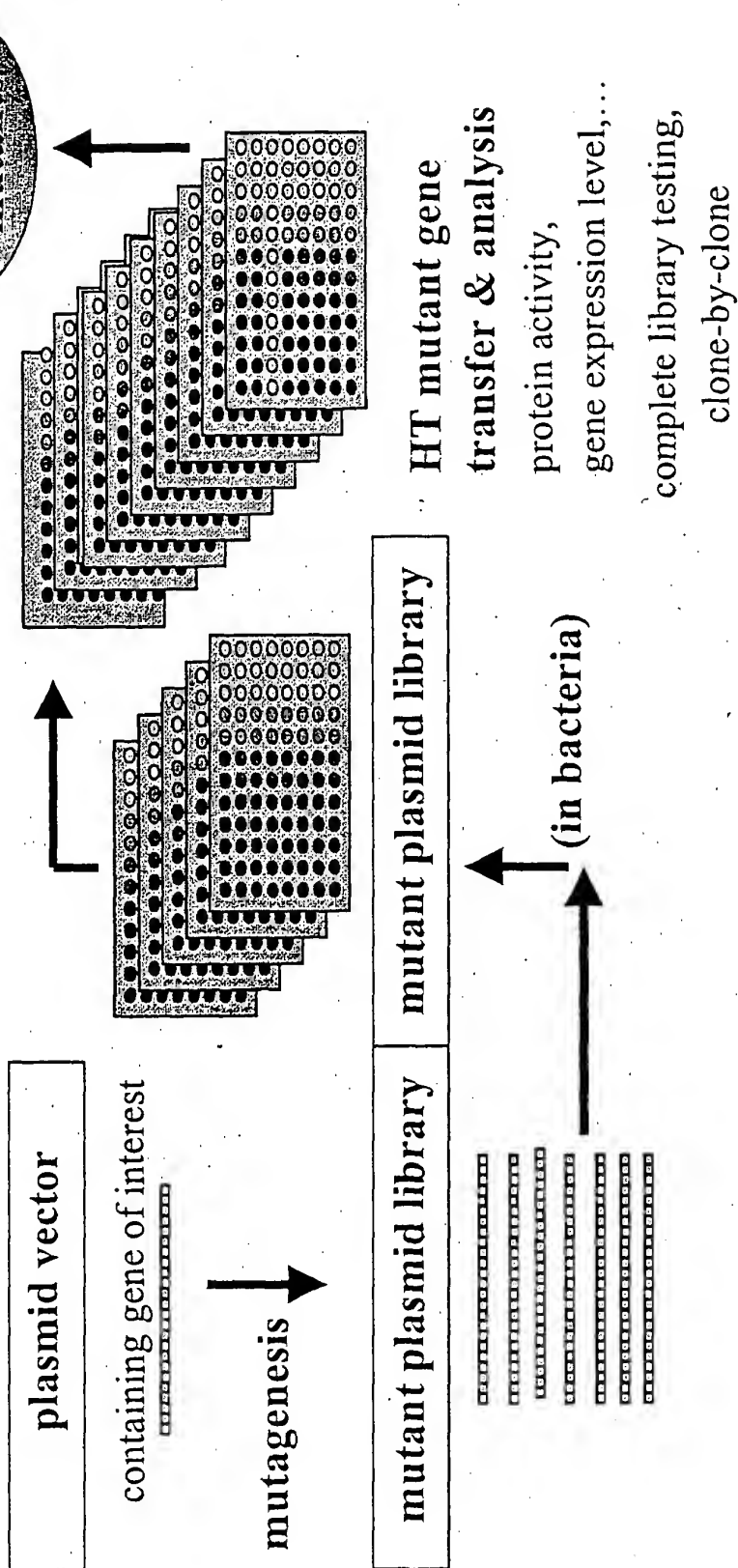
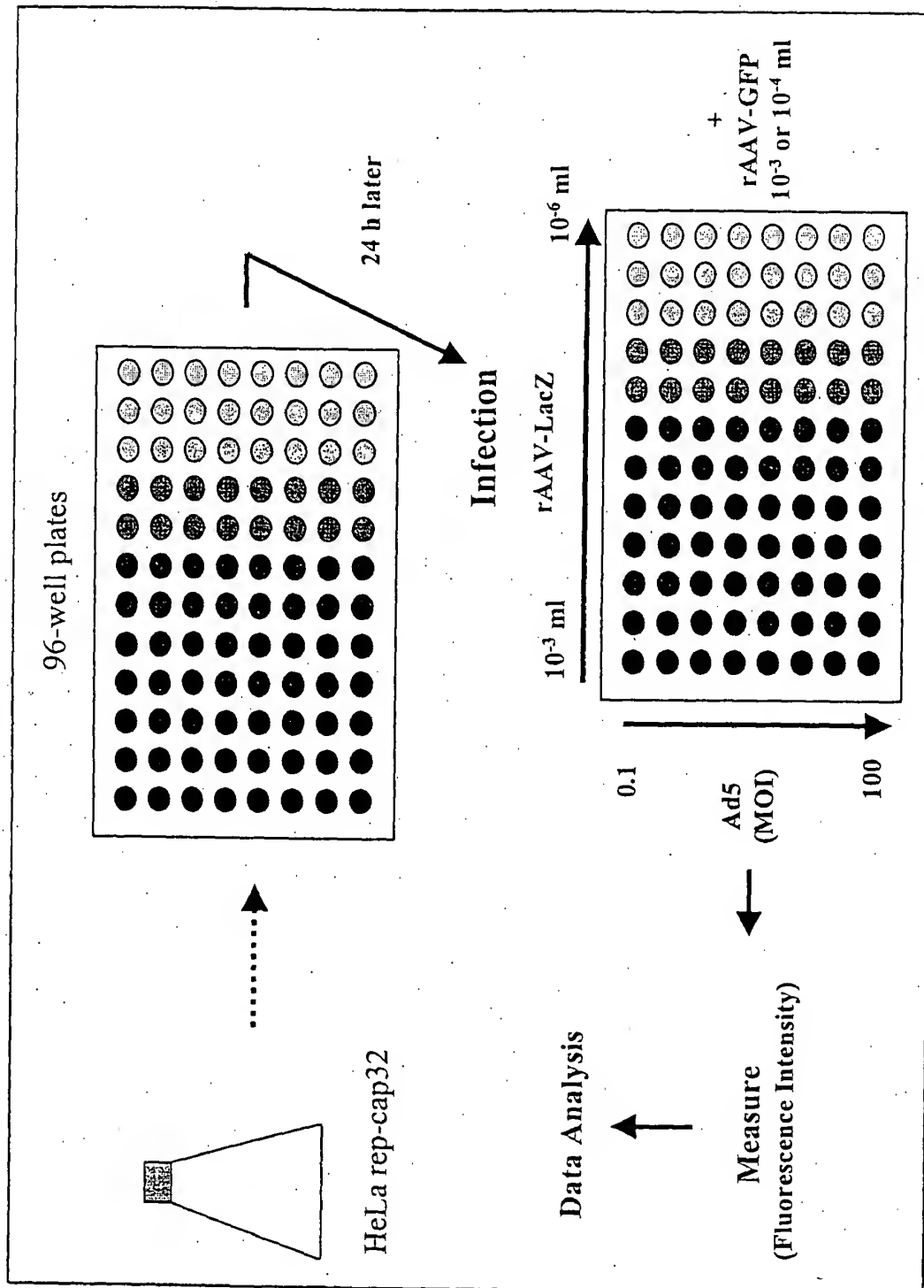


FIG. 2A

FIG. 2A



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FIG 7B

TREE AAV lacZ 1 μ l+AAV GFP 1 μ l

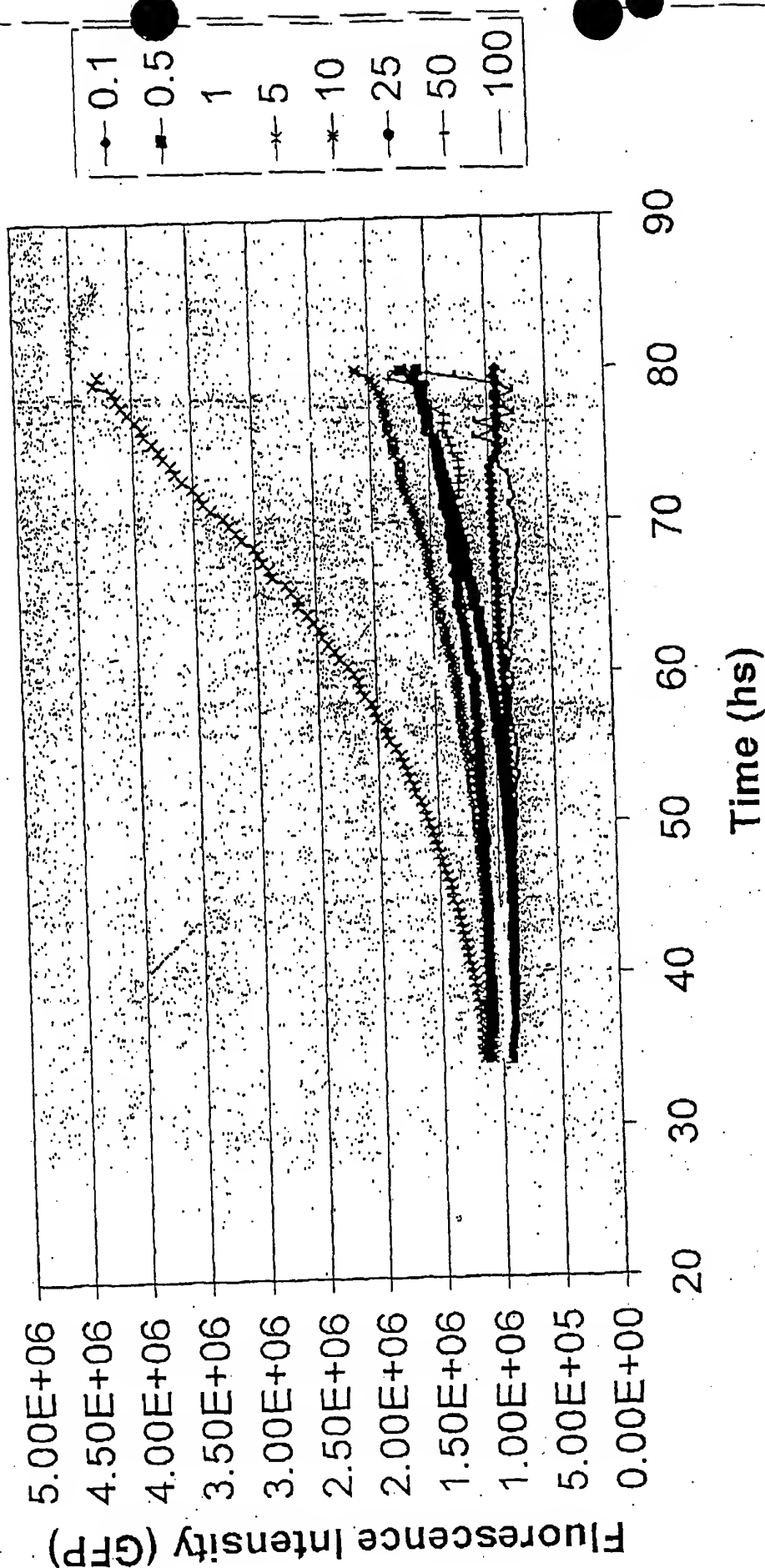


FIG. 2C

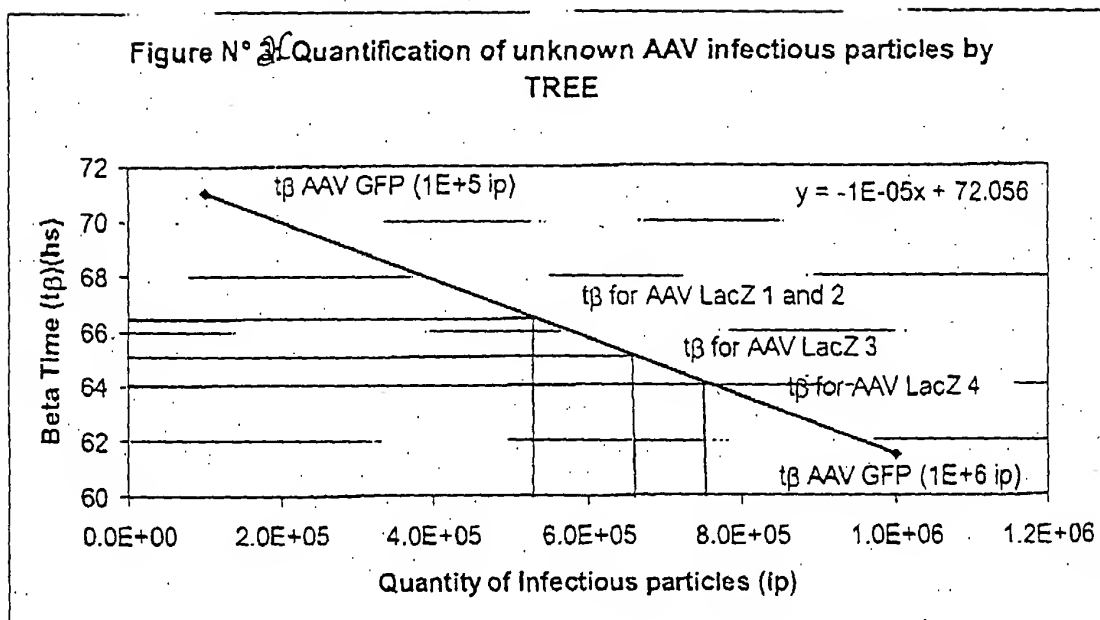


FIGURE 3A

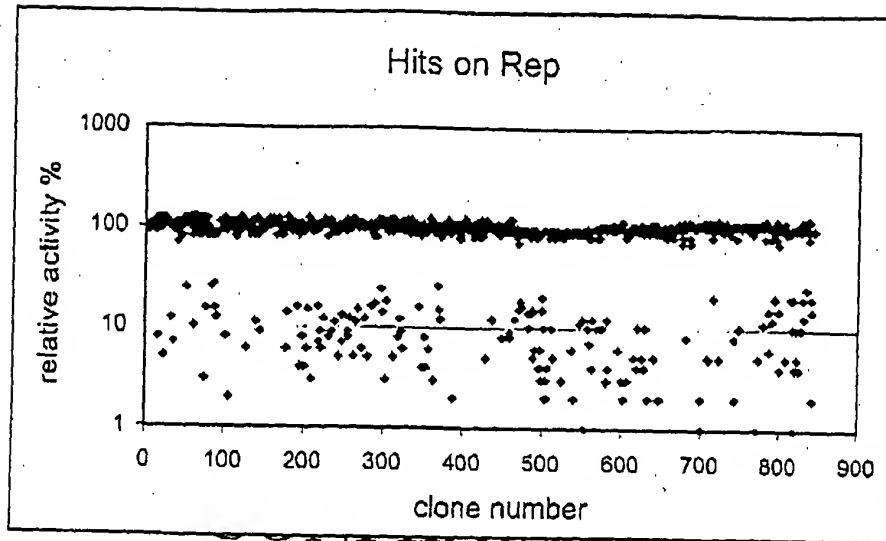


FIGURE 3B

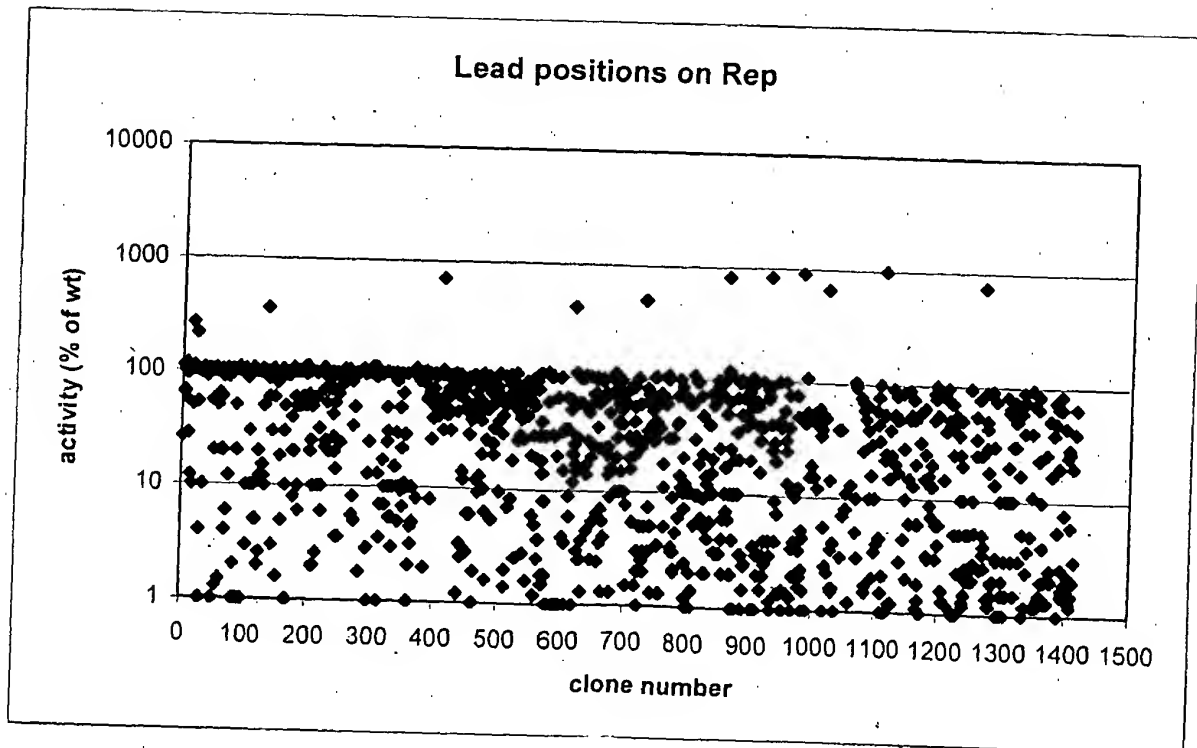


FIGURE 4

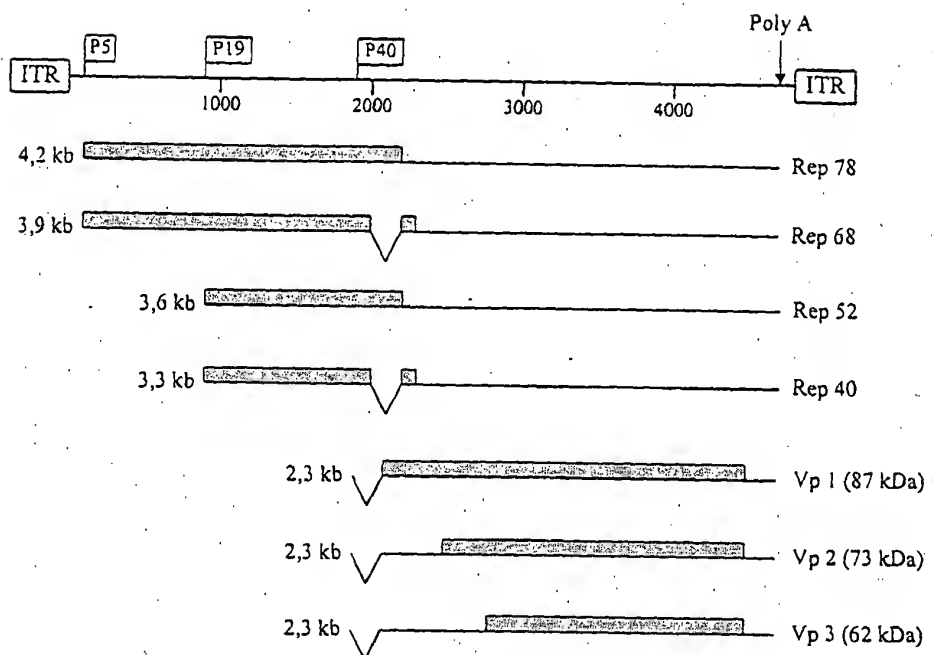


FIGURE 5A

```

      10      20      30      40      50      60
1  MPGFFEIVIKVPSDLDEHLPGISDSFVSWVAEKEWELPPDSMDLNLIEQAPLTVAEKLQ  60
2  MPGFFEIVIKVPSDLDEHLPGISDSFVNWVAEKEWELPPDSMDLNLIEQAPLTVAEKLQ  60
3  MPGFFEIVLKVPSDLDEHLPGISNSFVNWVAEKEWELPPDSMDPNLIEQAPLTVAEKLQ  60
4  MPGFFEIVLKVPSDLDEHLPGISNSFVNWVAEKEWELPPDSMDPNLIEQAPLTVAEKLQ  60
5  MPGFFEIVLKVPSDLDEHLPGISDSFVSWVAEKEWELPPDSMDLNLIEQAPLTVAEKLQ  60
6  MPGFFEIVIKVPSDLDEHLPGISDSFVNWVAEKEWELPPDSMDLNLIEQAPLTVAEKLQ  60
7  MATFFEIVIRVPFDVEEHLPGISDSFVDWVTGQIWELPPESDLNLTVEQPQLTVADRIR  60
C  M**FFE** : VP*D**HLPGIS+SFV : WV*****WELPP*SD***L*EQ**LTVA****

      70      80      90      100      110      120
1  RDFLVQWRRRVSKAPEALFFVQFEKGESYFHLHLVETTGVKSMVLGRFLSQIRDKLVQTI  120
2  RDFLVQWRRRVSKAPEALFFVQFEKGESYFHLHLVETTGVKSMVLGRFLSQIRDKLVQTI  120
3  REFLVEWRRRVSKAPEALFFVQFEKGETYFHLHLVLIETIGVKSMVVGGRYVSQIKEKLVTRI  120
4  REFLVEWRRRVSKAPEALFFVQFEKGETYFHLHLVLIETIGVKSMVVGGRYVSQIKEKLVTRI  120
5  REFLVEWRRRVSKAPEALFFVQFEKGDSYFHLHLVETVGVKSMVVGGRYVSQIKEKLVTRI  120
6  RDFLTEWRRRVSKAPEALFFVQFEKGESYFHMHLVETTGVKSMVLGRFLSQIREKLIQRI  120
7  RVFLYEWNNKFSKQ - ESKFFVQFEKGESEYFHLHLVETSGISSMVLGRYVSQIRAQLVKVV  119
C  R : FL++W***SK**E**FFVQFEK+ : YFH*H : L+ET : G**SMV : GR : : SQI : : *L* : : *

      130      140      150      160      170      180
1  YRGIEPTLPNWFVAVTKTRNGAGGKNKVVDDECYIPNYLLPKTQPELQWAWTNMEEYISACL  180
2  YRGIEPTLPNWFVAVTKTRNGAGGKNKVVDDECYIPNYLLPKTQPELQWAWTNMEEYISACL  180
3  YRGVPEQLPNWFVAVTKTRNGAGGKNKVVDDECYIPNYLLPKTQPELQWAWTNMDQYLSACL  180
4  YRGVPEQLPNWFVAVTKTRNGAGGKNKVVDDECYIPNYLLPKTQPELQWAWTNMDQYLSACL  180
5  YRGVPEQLPNWFVAVTKTRNGAGGKNKVVDDECYIPNYLLPKTQPELQWAWTNMDQYISACL  180
6  YRGIEPTLPNWFVAVTKTRNGAGGKNKVVDDECYIPNYLLPKTQPELQWAWTNMEQYLSACL  180
7  FGIEPQINDWVAITKVKK - GGANKVVD SGYIPAYLLPKVQPELQWAWTNLDEYKLAAL  177
C  **G : EP : ***W*A*TK*****GG*NKVVD : *YIP*YLLPK*QPELQWAWTN* : : Y : *A*L

      190      200      210      220      230      240
1  NLAERKRLVAQHLTHVSQTQEONKENLNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK  240
2  NLAERKRLVAHDLTHVSQTQEONKENLNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK  240
3  NLAERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK  240
4  NLAERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK  240
5  NLAERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK  240
6  NLTERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDKGITSEK  240
7  NLEERKRLVAQFLAESSQRS - QEAASQREFSADPVIKSKTSQKYMALVNWLVEHGITSEK  236
C  NL+ERKRLVA*+L***SQ***Q*****+***S**PVI*SKTS**YM*LV*WLV*+GITSEK

      250      260      270      280      290      300
1  QWIQEDQASYISFNAASNSRSQIKAALDNAGKIMALTKSAPDYLVGPPADIKTNRIYR  300
2  QWIQEDQASYISFNAASNSRSQIKAALDNAGKIMALTKSAPDYLVGPPADIKTNRIYR  300
3  QWIQEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYLVGSNPPEDITKNRIYQ  300
4  QWIQEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYLVGSNPPEDITKNRIYQ  300
5  QWIQEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYLVGQNPPEISSNRIYR  300
6  QWIQEDQASYISFNAASNSRSQIKAALDNAGKIMSLTKTAPDYLVGQPPVEDISSNRIYK  300
7  QWIQENQESYLSFNSTGNSRSQIKAALDNATKIMSLTKSAVDYLVGSSVPEDISKNIWQ  296
C  QWIQE*Q*SY*SFN**NSRSQIKAALDNA : KIM+LTK : A*DYLVG : : **+DI : : NRI* :

      310      320      330      340      350      360
1  ILELNGYDPAYAGSVFLGWAQKRFGKRNTIWLFGPATTGKTNIAEAIHAHVPFYGCVNWT  360
2  ILELNGYDPAYAGSVFLGWAQKRFGKRNTIWLFGPATTGKTNIAEAIHAHVPFYGCVNWT  360
3  ILELNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKTNIAEAIHAHVPFYGCVNWT  360
4  ILELNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKTNIAEAIHAHVPFYGCVNWT  360
5  ILEMNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKTNIAEAIHAHVPFYGCVNWT  360
6  ILELNGYDPQYAASVFLGWATKKFGKRNTIWLFGPATTGKTNIAEAIHAHTVPFYGCVNWT  360
7  ILEMNGYDPAYAGSILYGWCQRSFNKRNTVWLYGPATTGKTNIAEAIHAHTVPFYGCVNWT  356
C  I*E+NGY*P : YA : S***GW*** : F*KRNT*WL*GPATTGKTNIAEAIHAH+VPFYGCVNWT
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